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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

QAZI, SABIHA NAIM

ART UNIT

PAPER NUMBER

1616

DATE MAILED: 05/15/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/865,859

Applicant(s)

GERRITSEN ET AL.

Examiner

Sabiha Naim Qazi

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on 12 February 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☐ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) 5, 7, 8, 11, 15 and 17-29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 1-4, 6, 9, 10, 12-14 and 16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) 7-8, 11, and 17-29 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

### **First Office Action on Merits**

Claims 1-29 are pending.

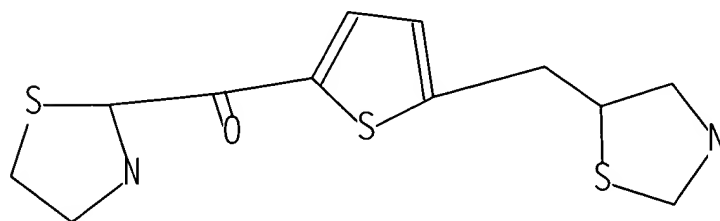
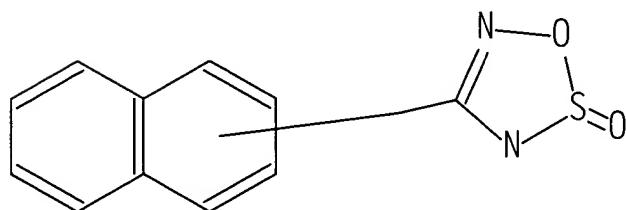
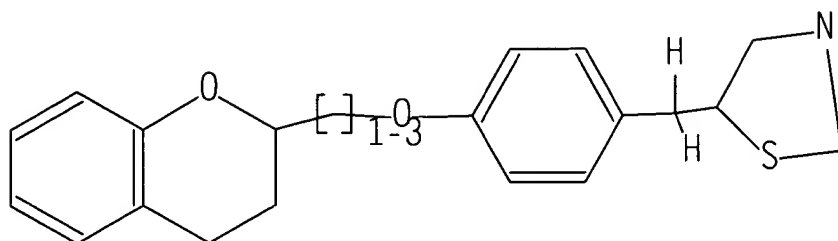
No claim is allowed.

Claims 1-4, 6, 9, 10, 12-14, 16 are examined; others are withdrawn from consideration as non elected invention.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Applicant's response filed in paper no. 5, dated 2/12/02 with election of group 1, (method of using the compound of formula 1), with traverse is hereby acknowledged. Furthermore, Applicants elected a species troglitazone, which is a benzopyran -2,4-thiazolidine dione derivative, namely (+)-5-((4-(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy)phenyl)methyl)-2,4-thiazolidione. Claims 5 and 15 are drawn to further comprising RXR receptor ligand which does not fall in group I, therefore, was not examined.

The traversal is on the ground(s) that the examiner has not shown how these groups are independent and distinct. This is not found persuasive because these groups have compounds of different formulas and hence structure.



Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and the search required for Group I is not required for any other Group and have acquired a

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separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

If applicant's traverse on the grounds that the inventions are not patentably distinct, applicants should submit evidence or identify such evidence now of record showing the groups to be obvious variants or clearly admit on the record that this is the case. In either instance if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 USC 103 of the other invention.

The requirement is still deemed proper and is therefore made FINAL.

***Information Disclosure Statement***

No IDS is filed in this application. If applicant wants to publish the references on the face of the file, IDS must be filed. An IDS should comply with 37 CFR 1.98(a) to include a concise explanation of the relevance.

References are not needed if they were submitted in the parent application.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 6, 9, 10, 12-14, and 16 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "comprising" cited in claims is inclusive and fails to exclude unrecited steps. The use of the term comprising to introduce claimed structure means that the ingredients covered by these claims may involve more elements than those positively recited. *Ex parte Gottzein et al.*, 168 USPQ 176 (PTO Bd. App. 1969). Comprising leaves the claim open for inclusion of unspecified ingredients even in major amounts. *Ex parte Davis et al.*, 80 USPQ 448 (PTO Bd. App. 1948).

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 9, 10, 12-14, 16 rejected under 35 U.S.C. 102(b) as being anticipated by Urban et al. (US Patent 5,814,647). See the abstract; lines 48-67, col. 1; lines 1-34, col. 2. ; examples 5, 6 and 8. Troglitazone is disclosed as a ligand for the orphan nuclear receptor PPAR Gamma. Translocation of this transcription factor in the nucleus of cells at sufficient rates inhibits transcription and reduces progesterone production in normal granulose cells without a loss of cell viability. However, this inhibition of transcription in rapidly dividing cancer cells expressing PPAR gamma results in the loss of cell viability and inhibition of cell growth.

Troglitazone and related compounds are disclosed for use in the treatment of cancer, to impair the growth of cancer cells without killing normal cells. See lines 40-43,

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col. 3. Method of inhibiting angiogenesis is not recognized by the prior art however; it discloses the use of troglitazone for treatment of tumor cells and cancer. See also examples 5, 6 and 8. All the elements are taught by the prior art.

See Exparte Novitski, 26 USPQ 2d 1389 (January 22, 1993) which is decision of USPTO Board of Appeals, holding to be inherent and not patentable, inoculating healthy plants with a known plant inoculant's, employed in the prior art to protect them against phytopathogenic fungi. Novitski discovered that the known plant inoculants would also protect them against root dwelling plant pathogenic nematodes, a discovery neither known nor appreciated by the prior art. The step of inoculating plants with the same inoculants necessarily and inherently protects them against nematodes.

2. See Atlas Powder versus Ireco, 51 USPQ 2d 1943, (Fed. Cir. 1999), holds the failure of those skilled in the art to contemporaneously recognize an inherent property, function, or ingredient of a prior art reference does not preclude a finding of anticipation. Whether or not an element is inherent in the prior art, is a fact question. Inherency is not necessarily conterminous with knowledge of those of ordinary skill in the art, who may not recognize the inherent characteristics or functioning of the prior art. However, the discovery of a previously unappreciated property of a prior art composition does not render the old composition new to the discoverer. The fact that prior art taught away from the claim is, in fact, only a showing that prior art did not recognize the inherent function. This lack of contemporary understanding did not defeat the showing of inherency.

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As is clear from the above discussion and citations that the instant invention is a known process of inhibition of tumor by troglitazone therefore is inherently taught by the prior art of record and other thiazolidine compounds,

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patent ability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patent ability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein



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were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**1. Determining the scope and contents of the prior art.**

Claims (1-4, 6, 9, 10, 12-14, 16) are rejected under 35 U.S.C. 103(a) as being unpatentable over Urban et al. (5,814,647) and Cushman et al. (J. Med. Chem. (1997), Vol 40, No. 15, 2323-2334). See the entire document especially lines 1-9, col. 3; lines 13-43; examples 5, 6 and 8; and figures 11 and 13; see in Cushman et al. lines 16-23 col. 1, page 2323) where angiogenesis is defined as the formation of new blood vessels required for the growth of solid tumors.

**2. Ascertaining the differences between the prior art and the claims at issue.**

Instant claims differ from the reference Urban et al. in claiming a method for inhibiting "angiogenesis" by the thiazolidinedione compounds of formula 1 (elected species is troglitazone) whereas prior art teaches use of troglitazone and related thiazolidinedione compounds as PPAR gamma ligand in the treatment of cancer (lines 1-5 and 13-22, col. 3; examples 5 and 6) and climacteric. Urban et al. does not use the term "angiogenesis " as in instant claims.

Cushman et al. teach that angiogenesis is the formation of new blood vessels required for the growth of solid tumors, (see lines 16-23, col. 1, page 2323).

**3. Resolving the level of ordinary skill in the pertinent art.**

Since Cushman et al. teach that angiogenesis is the formation of new blood vessels required for the growth of solid tumors, (see lines 16-23, col. 1, page 2323). Inhibition of angiogenesis is to stop the growth of tumor. Applicant is claiming method of inhibition of angiogenesis by troglitazone and Urban et. al. teach troglitazone for treatment of cancer, which is the inhibition of angiogenesis. Therefore, it would have been obvious to one skilled in the art at the time of invention to be motivated to use troglitazone for treatment of cancer and for inhibition of angiogenesis because angiogenesis is the formation of new blood vessels.

No tumor will be produced if the new formation of blood vessels is stopped by troglitazone.

**4. Considering objective evidence present in the application indicating obviousness or nonobviousness.**

Since troglitazone is disclosed as a ligand for the orphan nuclear receptor PPAR Gamma. Translocation of this transcription factor in the nucleus of cells at sufficient rates inhibits transcription and reduces progesterone production in normal granulose cells without a loss of cell viability. However, this inhibition of transcription in rapidly dividing cancer cells expressing PPAR gamma results in the loss of cell viability and inhibition of cell growth. Motivation is that Troglitazone and related compounds are disclosed for use in the treatment of cancer, to impair the growth of cancer cells without killing normal cells. See lines 40-43, col. 3 in Urban reference. One skilled in the art would use these compounds for the treatment of cancer, no matter mechanism of angiogenesis is not disclosed.

***Telephone Inquiry Contacts***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Naim Qazi whose telephone number is 703-305-3910. The examiner can normally be reached on First Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose Dees can be reached on 703-308-4628. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)-308-1235.

5/1/02



SABIHA QAZI, PH.D  
PRIMARY EXAMINER